

## SEQUENCE LISTING

<110> COHEN, STEPHEN  
BOUWMEESTER, ANTONIUS  
ROYET, JULIEN

<120> REGULATOR OF NOTCH SIGNALING ACTIVITY

<130> 55880 (71745)

<140> 09/830,980  
<141> 2001-05-02

<150> PCT/IB99/01891  
<151> 1999-11-03

<150> GB 9824045.0  
<151> 1998-11-03

<160> 16

<170> PatentIn Ver. 2.1

<210> 1  
<211> 480  
<212> PRT  
<213> Drosophila sp.

<400> 1  
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Ala Arg Leu Val Tyr Thr Gly Glu Glu Ala Gly Pro Pro Ile Asp Leu  
20 25 30

Pro Ala Gly Ile Thr Thr Gln Gln Leu Gly Leu Ile Cys Asn Ala Leu  
35 40 45

Leu Lys Asn Glu Glu Ala Thr Pro Tyr Leu Phe Phe Val Gly Glu Asp  
50 55 60

Glu Ile Lys Lys Ser Leu Glu Asp Thr Leu Asp Leu Ala Ser Val Asp  
65 70 75 80

Thr Glu Asn Val Ile Asp Ile Val Tyr Gln Pro Gln Ala Val Phe Lys  
85 90 95

Val Arg Pro Val Thr Arg Cys Thr Ser Ser Met Pro Gly His Ala Glu  
100 105 110

Ala Val Val Ser Leu Asn Phe Ser Pro Asp Gly Ala His Leu Ala Ser  
115 120 125

Gly Ser Gly Asp Thr Thr Val Arg Leu Trp Asp Leu Asn Thr Glu Thr  
130 135 140

Pro His Phe Thr Cys Thr Gly His Lys Gln Trp Val Leu Cys Val Ser  
 145 150 155 160  
 Trp Ala Pro Asp Gly Lys Arg Leu Ala Ser Gly Cys Lys Ala Gly Ser  
 165 170 175  
 Ile Ile Ile Trp Asp Pro Glu Thr Gly Gln Gln Lys Gly Arg Pro Leu  
 180 185 190  
 Ser Gly His Lys Lys His Ile Asn Cys Leu Ala Trp Glu Pro Tyr His  
 195 200 205  
 Arg Asp Pro Glu Cys Arg Lys Leu Ala Ser Ala Ser Gly Asp Gly Asp  
 210 215 220  
 Cys Arg Ile Trp Asp Val Lys Leu Gly Gln Cys Leu Met Asn Ile Ala  
 225 230 235 240  
 Gly His Thr Asn Ala Val Thr Ala Val Arg Trp Gly Gly Ala Gly Leu  
 245 250 255  
 Ile Tyr Thr Ser Ser Lys Asp Arg Thr Val Lys Met Trp Arg Ala Ala  
 260 265 270  
 Asp Gly Ile Leu Cys Arg Thr Phe Ser Gly His Ala His Trp Val Asn  
 275 280 285  
 Asn Ile Ala Leu Ser Thr Asp Tyr Val Leu Arg Thr Gly Pro Phe His  
 290 295 300  
 Pro Val Lys Asp Arg Ser Lys Ser His Leu Ser Leu Ser Thr Glu Glu  
 305 310 315 320  
 Leu Gln Glu Ser Ala Leu Lys Arg Tyr Gln Ala Val Cys Pro Asp Glu  
 325 330 335  
 Val Glu Ser Leu Val Ser Cys Ser Asp Asp Asn Thr Leu Tyr Leu Trp  
 340 345 350  
 Arg Asn Asn Gln Asn Lys Cys Val Glu Arg Met Thr Gly His Gln Asn  
 355 360 365  
 Val Val Asn Asp Val Lys Tyr Ser Pro Asp Val Lys Leu Ile Ala Ser  
 370 375 380  
 Ala Ser Phe Asp Lys Ser Val Arg Leu Trp Arg Ala Ser Asp Gly Gln  
 385 390 395 400  
 Tyr Met Ala Thr Phe Arg Gly His Val Gln Ala Val Tyr Thr Val Ala  
 405 410 415  
 Trp Ser Ala Asp Ser Arg Leu Ile Val Ser Gly Ser Lys Asp Ser Thr  
 420 425 430  
 Leu Lys Val Trp Ser Val Gln Thr Lys Lys Leu Ala Gln Glu Leu Pro  
 435 440 445

Gly His Ala Asp Glu Val Phe Gly Val Asp Trp Ala Pro Asp Gly Ser  
 450 455 460

Arg Val Ala Ser Gly Gly Lys Asp Lys Val Ile Lys Leu Trp Ala Tyr  
 465 470 475 480

<210> 2

<211> 1555

<212> DNA

<213> Drosophila sp.

<400> 2

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 actaccacgc aattggact gatttgcac ggcgtgtga aaaacgagga agccactcca 180  
 tatttgttt tcgtggcga ggatgagatc aagaagagcc tggaggacac gttggacttg 240  
 ggcgtcagtgg acaccgaaaa cgtgtatcgat attgtgtatc agccacagggc gttttcaaa 300  
 gtgcgcccag tgacaagatg cacgagttcc atgcgggac acgcccggc tgggtttcg 360  
 ctgaatttca gcccggatgg tgctcatctc gccagtggaa gtggcgacac cacagtgcga 420  
 ttgtggatc ttaacacaga gacaccgcac ttcacctgca caggtcataa gcagtgggtt 480  
 ctgtgcgtat cctgggtctc ggatggcaaa cgggtggca gccgttgcac agcgggctct 540  
 ataatcatct gggacccgga gacgggtcag cagaaggggc gacccttgag tgggcacaag 600  
 aaacacatca actgcctcgc ctgggaacccg tatcatcgcg atccggatgt cagggaaactt 660  
 gcttccgcca gtggagacgg ggactgcccgg atttggacg taaaattggg ccagtgcctt 720  
 atgaacatttgc cggacacac aaatgtgtg acagcagtga gatggggatgg agcgggctt 780  
 atttatacat cctccaaaga tcgcacagtg aagatgtggc gaggcagctga tggatctt 840  
 tgccggacgt tctctggca agctcactgg gtaaaacaaca ttgcgttgag caccgattac 900  
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 aacaagtgcg ttgagcgcac gacaggacac cagaacgtgg tcaacgtatgt gaaatattcg 1140  
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 agcgatggc agtacatggc caccttccgg ggtcatgtgc aggctgttta cacgttgcc 1260  
 tggccgcgg actccgcctt gattgttcc ggcagcaag actcaactct aaaagtatgg 1320  
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 gtggacttgg cggccgatgg ctcttagatgtt gcctctggtg gcaaggacaa agttataaag 1440  
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<210> 3

<211> 513

<212> PRT

<213> Saccharomyces cerevisiae

<400> 3

Met Ser Thr Leu Ile Pro Pro Pro Ser Lys Lys Gln Lys Lys Glu Ala  
 1 5 10 15

Gln Leu Pro Arg Glu Val Ala Ile Ile Pro Lys Asp Leu Pro Asn Val  
 20 25 30

Ser Ile Lys Phe Gln Ala Leu Asp Thr Gly Asp Asn Val Gly Gly Ala  
 35 40 45

Leu Arg Val Pro Gly Ala Ile Ser Glu Lys Gln Leu Glu Glu Leu Leu  
 50 55 60

Asn Gln Leu Asn Gly Thr Ser Asp Asp Pro Val Pro Tyr Thr Phe Ser  
 65 70 75 80

Cys Thr Ile Gln Gly Lys Lys Ala Ser Asp Pro Val Lys Thr Ile Asp  
 85 90 95

Ile Thr Asp Asn Leu Tyr Ser Ser Leu Ile Lys Pro Gly Tyr Asn Ser  
 100 105 110

Thr Glu Asp Gln Ile Thr Leu Leu Tyr Thr Pro Arg Ala Val Phe Lys  
 115 120 125

Val Lys Pro Val Thr Arg Ser Ser Ser Ala Ile Ala Gly His Gly Ser  
 130 135 140

Thr Ile Leu Cys Ser Ala Phe Ala Pro His Thr Ser Ser Arg Met Val  
 145 150 155 160

Thr Gly Ala Gly Asp Asn Thr Ala Arg Ile Trp Asp Cys Asp Thr Gln  
 165 170 175

Thr Pro Met His Thr Leu Lys Gly His Tyr Asn Trp Val Leu Cys Val  
 180 185 190

Ser Trp Ser Pro Asp Gly Glu Val Ile Ala Thr Gly Ser Met Asp Asn  
 195 200 205

Thr Ile Arg Leu Trp Asp Pro Lys Ser Gly Gln Cys Leu Gly Asp Ala  
 210 215 220

Leu Arg Gly His Ser Lys Trp Ile Thr Ser Leu Ser Trp Glu Pro Ile  
 225 230 235 240

Leu Val Lys Pro Gly Ser Lys Pro Arg Leu Ala Ser Ser Ser Lys Asp  
 245 250 255

Gly Thr Ile Lys Ile Trp Asp Thr Val Ser Arg Val Cys Gln Tyr Thr  
 260 265 270

Met Ser Gly His Thr Asn Ser Val Ser Cys Val Lys Trp Gly Gly Gln  
 275 280 285

Gly Leu Leu Tyr Ser Gly Ser His Asp Arg Thr Val Arg Val Trp Asp  
 290 295 300

Ile Asn Ser Gln Gly Arg Cys Ile Asn Ile Leu Lys Ser His Ala His  
 305 310 315 320

Trp Val Asn His Leu Ser Leu Ser Thr Asp Tyr Ala Leu Arg Ile Gly  
 325 330 335

Ala Phe Asp His Thr Gly Lys Lys Pro Ser Thr Pro Glu Glu Ala Gln  
 340 345 350

Lys Lys Ala Leu Glu Asn Tyr Glu Lys Ile Cys Lys Lys Asn Gly Asn  
 355 360 365  
 Ser Glu Glu Met Met Val Thr Ala Ser Asp Asp Tyr Thr Met Phe Leu  
 370 375 380  
 Trp Asn Pro Leu Lys Ser Thr Lys Pro Ile Ala Arg Met Thr Gly His  
 385 390 395 400  
 Gln Lys Leu Val Asn His Val Ala Phe Ser Pro Asp Gly Arg Tyr Ile  
 405 410 415  
 Val Ser Ala Ser Phe Asp Asn Ser Ile Lys Leu Trp Asp Gly Arg Asp  
 420 425 430  
 Gly Lys Phe Ile Ser Thr Phe Arg Gly His Ile Ala Ser Val Tyr Gln  
 435 440 445  
 Val Ala Trp Ser Ser Asp Cys Arg Leu Leu Val Ser Cys Ser Lys Asp  
 450 455 460  
 Thr Thr Leu Lys Val Trp Asp Val Arg Thr Arg Lys Leu Ser Val Asp  
 465 470 475 480  
 Leu Pro Gly Ile Lys Thr Lys Leu Tyr Val Asp Trp Ser Val Asp Gly  
 485 490 495  
 Lys Arg Val Cys Ser Gly Gly Lys Asp Lys Met Val Arg Leu Trp Thr  
 500 505 510

His

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<210> 4
<211> 351
<212> PRT
<213> Codonanthe elegans

<220>
<221> MOD_RES
<222> (184)..(185)
<223> Variable amino acid

<400> 4
Pro Gln Ile Ser Val Ser Glu Asp Glu Asn Glu Leu Gly Gly Ser Gly
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Ile Leu Val Pro Val Asp Ile Ser Thr Asn Glu Leu Gln Ile Leu Cys
  20          25          30

Asn Gln Leu Leu Gly Ser Arg Phe Cys Leu Asn Asn Glu Phe Ser Val
  35          40          45

Ser Gly Ala Glu Ile Val Asp Ser Ile Arg Lys Ser Leu Glu Glu Ile
  50          55          60
  
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Asp Phe Glu Thr Leu Lys Leu Val Tyr Gln Pro Gln Ala Val Phe Arg  
 65 70 75 80

Val Arg Pro Val Thr Arg Cys Ser Ala Ser Ile Pro Gly His Gly Glu  
 85 90 95

Pro Val Ile Ser Ala Gln Phe Ser Pro Asp Gly Arg Gly Leu Ala Ser  
 100 105 110

Gly Ser Gly Asp Gln Thr Met Arg Ile Trp Asp Ile Glu Leu Glu Leu  
 115 120 125

Pro Leu His Thr Cys Lys Ser His Lys Ser Trp Val Leu Cys Ile Ala  
 130 135 140

Trp Ser Pro Asp Ala Thr Lys Ile Ala Ser Ala Cys Lys Asn Gly Glu  
 145 150 155 160

Ile Cys Ile Trp Asn Ala Lys Thr Gly Glu Gln Ile Gly Lys Thr Leu  
 165 170 175

Lys Arg His Lys Gln Trp Ile Xaa Xaa Leu Ala Trp Gln Pro Thr Val  
 180 185 190

Lys Met Trp Arg Ala Asp Asp Gly Val Met Cys Arg Asn Met Thr Gly  
 195 200 205

His Ala His Trp Ile Asn Thr Leu Ala Leu Asn Thr Asp Tyr Ala Leu  
 210 215 220

Arg Thr Ser Cys Phe Glu Pro Ser Lys Ile Asn Arg Met Thr Gly His  
 225 230 235 240

Met Gln Leu Val Asn Gln Val Val Phe Ser Pro Asp Thr Arg Tyr Ala  
 245 250 255

Ser Ala Ser Phe Asp Lys Ser Val Lys Leu Trp Cys Gly Arg Thr Gly  
 260 265 270

Lys Tyr Leu Ala Ser Phe Arg Gly His Val Gly Pro Val Tyr Gln Val  
 275 280 285

Ala Trp Ser Ala Asp Ser Arg Leu Leu Val Ser Gly Ser Ala Asp Ser  
 290 295 300

Thr Leu Lys Val Phe Glu Leu Lys Thr Lys Ser Leu Tyr Tyr Asp Leu  
 305 310 315 320

Pro Gly His Gly Asp Glu Val Phe Thr Val Asp Trp Ser Pro Glu Gly  
 325 330 335

Thr Lys Val Val Ser Gly Gly Lys Asp Lys Val Leu Lys Leu Trp  
 340 345 350

&lt;210&gt; 5

&lt;211&gt; 103

<212> PRT  
 <213> Mus sp.

<220>  
 <221> MOD\_RES  
 <222> (39)  
 <223> Variable amino acid

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 1 5 10 15  
 Asp Glu Gly Gly Gln Leu Leu Gly Ser Pro Phe Asp Val Pro Val Asp  
 20 25 30  
 Ile Thr Pro Asp Lys Leu Xaa Leu Val Cys Asn Ala Leu Leu Ala Gln  
 35 40 45  
 Glu Glu Pro Leu Pro Leu Ala Phe Tyr Val His Asp Ala Glu Ile Val  
 50 55 60  
 Ser Ser Leu Gly Lys Thr Leu Glu Ser Gln Ser Val Glu Thr Glu Lys  
 65 70 75 80  
 Ile Val Asp Ile Ile Tyr Gln Pro Gln Ala Val Phe Arg Val Arg Ala  
 85 90 95  
 Val Thr Arg Cys Thr Ser Ser  
 100

<210> 6  
 <211> 78  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> MOD\_RES  
 <222> (66)  
 <223> Variable amino acid

<400> 6  
 Gly Ser Pro Phe Asp Val Pro Val Asp Ile Thr Pro Asp Arg Leu Gln  
 1 5 10 15  
 Leu Val Cys Asn Ala Leu Leu Ala Gln Glu Asp Pro Cys Pro Leu Ala  
 20 25 30  
 Phe Phe Val His Asp Ala Glu Ile Val Ser Ser Leu Gly Lys Thr Leu  
 35 40 45  
 Glu Ser Gln Ala Val Glu Thr Glu Lys Val Leu Asp Ile Tyr Gln Pro  
 50 55 60  
 Gln Xaa Leu Phe Arg Val Arg Ala Val Thr Arg Cys Thr Ser  
 65 70 75

<210> 7  
 <211> 476  
 <212> PRT  
 <213> Xenopus laevis

<400> 7  
 Met Lys Glu Asp Val Gly Arg Leu Leu Ile Gln Phe Lys Asn Glu Asn  
 1 5 10 15

Gly Glu Gly Leu Gly Thr Pro Phe Asp Val Pro Leu Asp Ile Thr Pro  
 20 25 30

Asp Lys Leu Gln Leu Val Cys Asn Ala Leu Leu Gln Glu Asp Pro  
 35 40 45

Val Pro Leu Ala Phe Phe Val Gln Asp Leu Glu Ile Val Thr Ser Leu  
 50 55 60

Asp Lys Thr Leu Glu Lys Gln Ser Val Glu Thr Glu Lys Val Ile Asp  
 65 70 75 80

Ile Ile Tyr Gln Pro Gln Ala Val Phe Lys Val Arg Ala Val Thr Arg  
 85 90 95

Cys Thr Ser Ser Leu Glu Gly His Thr Glu Ala Val Ile Ser Val Ala  
 100 105 110

Phe Ser Pro Thr Gly Lys Tyr Leu Ala Ser Gly Ser Gly Asp Thr Thr  
 115 120 125

Val Arg Phe Trp Asp Leu Ser Thr Glu Thr Pro His Phe Thr Ser Lys  
 130 135 140

Gly His Thr His Trp Val Leu Ser Ile Ala Trp Ser Pro Asp Gly Lys  
 145 150 155 160

Lys Leu Ala Ser Gly Cys Lys Asn Ser Gln Ile Phe Ile Trp Asp Pro  
 165 170 175

Ser Thr Gly Lys Gln Ile Gly Lys Pro Leu Thr Gly His Ser Lys Trp  
 180 185 190

Ile Thr Trp Leu Cys Trp Glu Pro Leu His Leu Asn Pro Glu Ser Arg  
 195 200 205

Tyr Leu Ala Ser Ala Ser Lys Asp Cys Thr Ile Arg Ile Trp Asp Thr  
 210 215 220

Val Met Gly Gln Cys Gln Lys Ile Leu Thr Ser His Thr Gln Ser Val  
 225 230 235 240

Thr Ala Val Lys Trp Gly Gly Asp Gly Leu Leu Tyr Ser Ser Ser Gln  
 245 250 255

Asp Arg Thr Ile Lys Ala Trp Arg Ala Gln Asp Gly Val Leu Cys Arg  
 260 265 270

Thr Leu Gln Gly His Ala His Trp Val Asn Thr Met Ala Leu Ser Thr  
 275 280 285  
 Asp Tyr Val Leu Arg Lys Gly Ala Phe Asn Pro Ala Asp Ala Ser Val  
 290 295 300  
 Asn Pro Gln Asp Met Ser Gly Ser Leu Glu Val Leu Lys Glu Lys Ala  
 305 310 315 320  
 Leu Lys Arg Ser Asn Glu Val Arg Gly Gln Gly Pro Glu Arg Leu Val  
 325 330 335  
 Ser Gly Ser Glu Asp Phe Thr Leu Phe Leu Trp Ala Pro Ala Glu Glu  
 340 345 350  
 Lys Lys Pro Leu Gln Arg Met Thr Gly His Gln Ala Leu Ile Asn Glu  
 355 360 365  
 Val Leu Phe Ser Pro Asp Thr Arg Ile Ile Ala Ser Ala Ser Phe Asp  
 370 375 380  
 Lys Ser Ile Lys Leu Trp Asp Gly Lys Thr Gly Lys Phe Leu Thr Ser  
 385 390 395 400  
 Leu Arg Gly His Val Ser Ala Val Tyr Gln Ile Ala Trp Ser Ala Asp  
 405 410 415  
 Ser Arg Leu Leu Val Ser Gly Ser Ser Asp Ser Thr Leu Lys Val Trp  
 420 425 430  
 Asp Ser Lys Thr Lys Lys Leu Leu Ile Asp Leu Pro Gly His Ala Asp  
 435 440 445  
 Glu Val Tyr Ser Val Asp Trp Ser Pro Asp Gly Gln Arg Val Ala Ser  
 450 455 460  
 Gly Gly Lys Asp Lys Cys Leu Arg Ile Trp Arg Lys  
 465 470 475

<210> 8  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: HA epitope

<400> 8  
 Tyr Pro Tyr Asp Val Pro Asp Tyr Ala  
 1 5

<210> 9  
 <211> 149

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<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 9
cgatccaaa aatgtatcc ctatgacgtc cccgattatg cttaccctta cgatgtacct 60
gactacgcgt atccgtacga cttccggac tatgctcagg agacggacac ggagcaagag 120
gccacgcccac atacataca ggcgcgcca 149

<210> 10
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 10
taaacgaggc gcgcctatcg tat 23

<210> 11
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<220>
<221> modified_base
<222> (12)
<223> i

<220>
<221> modified_base
<222> (21)
<223> i

<220>
<221> modified_base
<222> (24)
<223> i

<220>
<221> modified_base
<222> (27)
<223> i

<400> 11
cgcagaattc cttttttttt nccngtngay at 32

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<210> 12  
<211> 32  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Primer

<220>  
<221> modified\_base  
<222> (15)  
<223> i

<220>  
<221> modified\_base  
<222> (24)  
<223> i

<400> 12  
ggtgctcgag cytgnnggtg rtanatdatr tc

<210> 13  
<211> 8  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Conserved peptide

<400> 13  
Pro Phe Asp Val Pro Val Asp Ile  
1 5

<210> 14  
<211> 7  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Conserved peptide

<400> 14  
Asp Ile Ile Tyr Gln Pro Gln  
1 5

<210> 15  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Primer

<400> 15  
caccagataa actgcagtta g 21

<210> 16  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Primer

<400> 16  
ctgtttcaac tgattgcttc t 21